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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/288,837	04/08/1999	GENE H. MACDONALD	5470-238	7924

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/288,837	Applicant(s) MACDONALD ET AL.	
	Examiner Zachariah Lucas	Art Unit 1648	

-- The MAILING DATE of this communication appears on the cover she t with th correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 April 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *84,85,89-93 and 95-114* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *84,85,89-93 and 95-114* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *32* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Claims 84, 85, 89-93, and 95-114 are pending and under consideration in the present application. In the prior action, mailed on October 22, 2002, claims 84, 85, 89-93, and 95-104 were pending and rejected. Since that rejection, the Applicant has filed two Responses. A first Response on February 24, 2003, and a Supplemental Response, filed on April 25, 2003 in response to the April 16, 2003 interview. In the Responses, claims 84 and 95 have been amended twice, claims 91, 92, and 100-104 have been amended once, claims 105-114 have been added, and claim105 amended once.

Information Disclosure Statement

2. The information disclosure statement (IDS) submitted on April 11, 2003 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement has been considered by the examiner. However, as the submission consists of a listing of slides, without the slides described therein, the information has only been considered to the extent of the list.

Specification

3. **(Prior Objection- Withdrawn)** The specification was objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required: Claims 103 and 104 refer to Her2/neu gene products. However, the specification describes only the Her2 gene. See e.g. p. 9, lines 23-28; and

p. 17, lines 33-34. In view of the amendment of the claims to conform to the language of the specification, thereby negating the antecedent basis problem, the objection is withdrawn.

Claim Objections

4. **(Prior Objection-Withdrawn)** Claim 95 was objected to in the prior action because of the following informalities: In amending the claim, although the applicant overcame the 112 rejection regarding the phrase "an immunogenically effective amount", by identifying the amount as effective "to prevent or treat cancer" the applicants both inserted the phrase "an amount effective to" and kept the phrase "immunogenically effective amount." In view of the amendment canceling the phrase "an amount effective to," the objection is withdrawn.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. **(Prior Rejection-Withdrawn)** Claims 84, 85, and 90-93 were rejected in the prior action under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This rejection is withdrawn in view of the Supplemental Declaration by Robert A. Olmsted, submitted on April 11, 2003, which demonstrates that the administration of VEEV replicon particles, encoding the rat neu gene product, was effective in preventing cancer in mice transgenic for the rat neu gene.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. **(Prior Rejection- Withdrawn)** In the Action of November 26, 2001 (the prior action), claims 84, 85, 90-93, and 95-102 were rejected under 35 U.S.C. § 112, ¶ 2 for indefiniteness. There were two bases for this rejection. First, the claims were rejected because the phrase "an immunogenically effective amount" was indefinite as not stating what the amount was effective for. One reading the claim would not know the metes and bounds of the claimed invention because hey would not know what amounts were claimed. This rejection was overcome by the applicants' amendments of the claims in Amend. E. The amended claims state that the claimed compositions comprise the claimed alphavirus particles in an immunogenically effective amount to prevent or treat cancer.

The second basis for rejecting the claims under 35 U.S.C. 112 ¶ 2 was that the phrase "native cancer cell antigen" is indefinite. This part of the rejection was maintained in the prior action. However, in view of the amendment to the claims, and the statements in the Supplemental Response, amending and clearly defining what is meant by the new claim language regarding "naturally occurring cancer antigens," the rejection is hereby withdrawn.

9. **(Prior Rejection-Withdrawn)** Claims 103 and 104 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These claims have been amended to

make the claim language consistent with the language in the specification. The rejection is therefore withdrawn.

Claim Rejections - 35 USC § 102

10. **(Prior Rejection- Maintained in Part)** Claim 84, 85, 92, 93, 95, 96, 98, 100, and 102 were rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent Number 5,843,723, issued to Dubensky et al. These claims read on recombinant alphavirus vectors comprising native cancer cell antigens, including embodiments wherein the virus is the Venezuelan equine encephalitis virus (VEEV). This rejection is withdrawn in view of the Applicant's arguments in the Responses, and during the interview of April 16, 2003. In specific, the applicant's traversed the rejection by pointing out the distinction between the particles of Dubensky and the present application. The Applicant described Dubensky as teaching alphavirus particles which lack the genes encoding the structural proteins, thus rendering the particles unable to propagate. However, the invention described in the claims identified above use attenuated viruses, which are able to replicate, but at reduced levels.

However, while the Applicant's traversal is persuasive with regards to the claims identified above, which require that the replicon particles be attenuated particles, was persuasive, the same argument does not appear to apply to claims 105, 106, 109, 110, 111, and 114. These claims teach alpha virus (including VEEV) replicon vectors that infect antigen-presenting cells. They are not limited to replicon vectors with attenuated phenotypes, but to replicon vectors generally. In the specification, at page 18, the Applicant has identified a number of patents

disclosing examples of replicon vectors. Among those patents is the Dubensky patent, thereby indicating that the particles disclosed therein are in fact considered replicon vectors within the scope of the present invention. Therefore, in view of the broader scope of these later claims, and the fact that the Dubensky replicons are explicitly identified by the Applicant as replicon, the Dubensky vectors fall within the claim language. As for the requirement that the vectors infect antigen –presenting cells, including dendritic cells, page 8 of the application teach that the VEEV particles inherently infect such antigen-presenting cells. Thus, this claim limitation does not distinguish from the VEEV particles of Dubensky because that ability is taught to be inherent to the viral particles.

Claim Rejections - 35 USC § 103

11. **(Prior Rejection- Restated and Maintained)** Claims 84, 85, 90-93, and 95-104 were rejected under 35 U.S.C. 103(a) as being unpatentable over either 1) Johnston et al., WO 95/32733 or 2) U.S. Patent Number 5,843,723, issued to Dubensky et al. in view of U.S. Patent 5,792,462, issued to Johnston et al. (Johnston 2), with either 1 or 2 further in view of Falo et al., U.S. Patent Number 5,951,975. This rejection is maintained, and extended to claims 105-114 over the teachings of Dubensky in view of the Johnston references. The Applicant has amended the claims such that they now read on the use of naturally occurring cancer antigens as defined in by the applicant in the Supplemental Response filed on April 25, 2003. Such antigens include "antigenically similar molecules" to the naturally occurring cancer antigen. The amendment, which serves to clarify what was meant by a "native cancer cell antigen," also distinguishes

between the antigens taught by Falo, and the ones used in the present application. However, it is noted that the Examiner erred in his statement of the teachings of Dubensky in the prior action. As indicated above, and in the prior action in the 102 rejection over Dubensky, the reference teaches the use of cancer cell antigens that appear to fall within the scope of the presently rejected claims. Specifically, it teaches the use of cancer cell antigens to induce an immune response against cancer cells. See, column 19, lines 1-14, and columns 23-24. However, although the reference does teach replicon vectors expressing a native cancer cell antigen (see above), it does not teach the use of attenuated replicon particles.

However, while Dubensky does not teach attenuated replicon particles, it does teach the use of infectious viral particles to induce an immune response in a person against a cancer antigen. Each of the Johnston references teaches attenuated alphavirus particles for the use of inducing an immunogenic response against a heterologous antigenic protein encoded by a heterologous nucleic acid inserted into the replicon genome. See e.g., the abstracts of the two documents. The Johnston 2 reference also teaches, as was indicated in the prior action, that such attenuation renders the vectors unable to causing disease in the hosts. Col. 1, lines 40-59, and col. 6, lines 28-35. From the teachings of these references, it would have been apparent that the reason for deleting the genes encoding the structural genes from the replicon of Dubensky would be to achieve the same purpose as was achieved through the attenuating mutations of the Johnston references. It would therefore have been obvious to those of ordinary skill in the art to have used the attenuated vectors of the Johnston references in place of the inactivated vector of Dubensky.

New claims 108 and 113 further limit the claimed replicon particles to embodiments wherein the heterologous gene is associated with an alphavirus 26S subgenomic promoter. The Dubensky reference is described above. Although it teaches that the 26S subgenomic region encodes the structural proteins, it does not specifically teach the use of the 26S subgenomic promoters to express the heterologous genes. However, such would have been obvious to those of ordinary skill in the art due to the teachings of Johnston.

The Johnston references teach the use of VEEV vectors that express immunogenic heterologous genes operatively associated with the 26S subgenomic promoters. See e.g., abstracts. Because one of ordinary skill in the art would have known that these promoters were useful for the expression of immunologic heterologous proteins in VEEV vectors, it would have been obvious to use these promoters to express the heterologous cancer antigens of Dubensky.

12. **(New Rejection-Necessitated by Amendment)** Claims 84, 85, 90-93, and 95-115 are rejected under 35 U.S.C. 103(a) as being unpatentable over Weiner et al., U.S. Patent 6,468,982, in view of the Johnston references. The rejected claims have been described above. They have been amended such that they now read on naturally occurring cancer antigens that need not be native to the recipient host. Weiner teaches that genetic constructs that induce the expression of the neu gene in a cell can induce an immune response against hyperproliferative diseases including cancers. Column 14. Among the genes indicated by the reference as useful for the induction of the immune response is the neu gene. Col. 14, lines 55-56. The patent does not teach the use of viral vectors to deliver these genetic constructs. However, the teachings of Johnston references as described above, and in the prior actions, teach alphavirus vectors usable for the

delivery of nucleic acids encoding antigenic peptides to host cells. Thus, it would have been obvious to those in the art to have used the viral vectors of the Johnston references to deliver the genes/nucleic acids as described by the Weiner reference.

It is noted that the Weiner reference indicates that the described constructs represent an advance over the use of viral vectors. Columns 3-4. However, this is not deemed to teach away from the use of other, older viral vectors. The development of new inventions to perform the same or similar function does not make older technology any less obvious to those of ordinary skill in the art, and does not teach away from the prior invention in the sense of rebutting the motivational element of establishing obviousness. See e.g. In re Gurley, 31 U.S.P.Q. 2d 1130, 1131-1132 (Fed. Cir. 1994). The Federal Circuit stated in Gurley that a "known or obvious composition does not become patentable simply because it has been described as somewhat inferior to some other product for the same use." Id., at 1132. In short, the court held that teaching a better solution to problem is not a teaching away from a previously known, and operable, solution. Thus, although the Weiner reference teaches advantages of their method of genetic delivery over viral vectors, the reference does not teach away from the use of such.

Examiner's Note

13. It is noted that Dubensky teaches that the cancer antigens, if tumorigenic, must be rendered non-tumorigenic in order to be used. However, as the reference is also teaching the use of the cancer antigens to induce an immune response against cancer cells, the antigens must retain the ability to induce such a response. The Applicant has amended the claims to read on native cancer cell antigens, and defined the term as including both antigens that are found on

naturally occurring cancer antigens and "antigenically similar molecule." While this amendment effectively avoids the teachings of Falo, it does not appear to do the same for Dubensky.

Conclusion

14. No claims are allowed.

15. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 703-308-4240. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4027. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Z. Lucas
Patent Examiner
June 30, 2003

JAMES HOUSEL 6/30/03
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